Lymphocyte Predominant B-cell Lymphoma (NLPBL). Nodular sclerosis, mixed cellularity, lymphocyte depletion, and lymphocyte–rich HL are subgroups of classical HL. Risk Stratification An accurate assessment of the stage of disease in patients with HL is critical for the selection of the appropriate therapy. Prognostic models that identify patients at low or high risk for recurrence, as well as the response to therapy as determined by Positron Emission Tomography (PET) scan, are used to optimize therapy. Risk–Adapted Therapy Initial therapy for HL patients is based on the histology of the disease, the anatomical stage and the presence of poor prognostic features. Patients with early–stage disease are typically treated with combined modality strategies utilizing abbreviated courses of combination chemotherapy followed by involved–field radiation therapy, whereas those with advanced stage disease receive a longer course of chemotherapy often without radiation therapy. However, newer agents including brentuximab vedotin and anti–PD–1 antibodies are now standardly incorporated into frontline therapy. Management of Relapsed/Refractory Disease High–Dose Chemotherapy (HDCT) followed by an Autologous Stem Cell Transplant (ASCT) is the standard of care for most patients who relapse following initial therapy. For patients who fail HDCT with ASCT, brentuximab vedotin, PD–1 blockade, non–myeloablative allogeneic transplant or participation in a clinical trial should be considered. The AETHERA study (NCT01100502) shows that Brentuximab Vedotin (BV) improves Progression-Free Survival (PFS) after ASCT in patients with Refractory or Relapsed HL (R/R HL). For patients who relapse after ASCT, BV, and anti-PD-1, monoclonal antibodies were considered incurable, and their outcome is rather dismal, with a median Overall Survival (OS) of 2-years. For Refractory or Relapsed cHL (R/R cHL) patients who have failed both ASCT and BV, Chimeric Antigen Receptor T-cell (CAR-T) therapy offers a new therapeutic option.

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08

HISTORY OF BLOOD TRANSFUSION

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It is not easy to cover the history of transfusion in all its aspects. In the era when blood transfusion was first tried, the indications for blood transfusion were also very different: mental illness, gaining strength, rejuvenation, etc. Blood transfusion process has gone through many dangerous and difficult stages, from obtaining the blood to its safe application in peace, in war, and in the laboratory. This presentation focuses on some stages and developments in the application of blood transfusion. The main developments are summarized in Table 1. The main problems encountered in the history of transfusion can be summarized as follows:

- Blood clotting and preservation could be prevented by the use of 0.2% sodium citrate and dextrose.
- Severe transfusion reactions could mostly be prevented after the ABO blood groups were identified.
- Infection problems that could be partially controlled with antiseptic agents.

In this presentation, various obstacles encountered in the history of blood transfusion and developments regarding their solutions are presented.

Table 1 Important stages in the history of blood transfusion.

1628	William Harwey (GB)	Discovery of human blood circulatory system
1666	Richard Lower (Oxford)	Experiments of blood transfusion beetween animals
1667	Jean Denis (Paris)	Transfusion blood from animals to humans
1818	James Blundell (London)	First blood transfusion from one human to another
1854	J Bovell E Hodder (Toronto)	Cow's milk transfusions was first attempted
1901	Karl Landsteiner (Wienna)	Discovery of ABO blood groups (Nobel Prize in 1930)
1915	Richard Lenwinsohn (NY)	Developing 0.2% sodium citrate as anticoagulant
1921	Percy Oliver (London)	The first blood donor service is established
1932	in the SU and the USA	Cadaveric blood began to be used
1937	Bernard Fantus (Chicago)	The first blood bank
1940	Edwin Cohn (Boston)	A method for fractionation of plasma proteins
1951	Edwin Cohn (Boston)	Developping the first blood cell separator
1971		Hepatitis B surface antigen testing of donated bloods
1982	J Goldstein	Developing universal type O blood by enzyme treatment
1983	L. Montaignier (Paris)	Isolation of the virus that causes AIDS
From 1987 to 2008		A series of tests are developed to screen donated blood for infectious diseases
2010	Seifinejad A et al.	RBCs generated from human induced pluripotent SCs
2020	Ebrahimi M, et al.	Differentiation of human induced pluripotent stem cells into RBCs

SU, Soviet Union; USA, United States of America; RBCs, Red Blood Cells; SCs, Stem Cells.

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09

TREATMENT FOR HODGKIN'S LYMPHOMAS IN COUNTRIES WITH LIMITED RESOURCES

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The incidence and long-term clinical outcome of Hodgkin Lymphoma (HL) vary according to different patient, disease-related factors and geographic location. There have been

dramatic changes in the staging and treatment of Hodgkin's Lymphoma (HL) over the last two decades. 75%–80% of patients with classical HL can achieve long-term remission with contemporary risk-adapted frontline therapy in high income countries. However, 25%–30% of patients with advanced-stage disease experience relapse or have primary refractory disease. For patients with Relapsed/Refractory HL (rrHL), salvage therapy followed by Stem Cell Transplantation (SCT) is the current standard of care. Despite the significant improvement in the diagnosis, staging, the use of risk-adapted approach, introduction of novel agents (CPI, Bv) in frontline setting, the use of post-transplant consolidation maintenance therapy, 50% of patients still experience disease progression, with poor prognosis and shortened survival. Most of the real-world data regarding treatment pathways and clinical outcomes in relapsed refractory HL published from high income countries in Euro and North America. There is a limited data on clinical characteristics and clinical outcomes of HL in low-resourced countries. Very few studies published so far with limited number of patients, single-center experiences, poor data quality, or lack of comprehensive information on patients, treatment, or clinical outcomes. In my presentation, we will highlight the disease entity from diagnosis, staging to treatment options worldwide; the availability and the use of novel agents in frontline and in relapsed refractory setting, availability of stem cell transplantation procedures and compare the clinical outcomes of HL patients in both high- and low-resourced countries.

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10

CLASSIFICATION OF MPN

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The 2022 updated 5th edition of the World Health Organization Classification of myeloproliferative neoplasms and mastocytosis focused on changes in the rationale behind the classification, combined morphologic, immunophenotypic, molecular, and cytogenetic data that help to refine diagnostic criteria and emphasize therapeutically and/or prognostically actionable biomarkers. While a genetic basis for defining diseases is sought where possible, the classification strives to keep practical applicability in perspective. In addition, a new International Consensus Classification (ICC) has been introduced for myeloid neoplasms and acute leukemia. In the context of MPN, the classical subtypes of MPN remained unchanged; however, the experts made an effort to refine the diagnostic criteria to allow a distinction between subtypes. With refinement of the diagnostic criteria, the hope is that clinicians will be able to distinguish between specific subtypes with greater accuracy and present a more definitive and holistic management for patients from diagnosis through disease monitoring.

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11

PREDİCTİON OF THE RİSK OF LEUKEMİA DEVELOPMENT İN AGED HEALTHY POPULATİON: IMPLEMENTATİON İN THE PUBLİC HEALTH SYSTEM

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In the last 10-years, several scientific reports have provided evidence of the accumulation of somatic mutations in Hematopoietic Stem and Progenitor Cells (HSPC) in subjects aged > 50yrs. This phenomenon is defined as Clonal Hematopoiesis of Indeterminate Potential (CHIP). As discovered and developed by Abelson et.al. (Nature. 2018) these mutations are detectable many years before the clinical onset of Acute Myeloid Leukemia (AML) and are potentially linked to its subsequent evolution. It is important to underline that the correlation between mutations and the development of AML does not represent an early diagnosis but only an increased risk of developing AML. The risk depends on many factors: type of mutations, how many cells carry the mutation, and combination of mutations. A risk score has been established (NEJM 2023); according to this study few subjects with CHIP are going to develop AML. Of note: the studies that document these correlations were retrospective. It might be relevant to emphasize that "early diagnosis of AML" does not seem to have, given the dynamics of cellular proliferation, concrete advantages. The identification early in advances of a constellation of mutations and their combinations possibly associated with the risk of developing AML could instead be very effective, if there were drugs targeting specific mutations. From a precision, personalized and participatory medicine perspective, these studies have led us to launch a prospective project on a healthy population of individuals between 50 and 80-years old. We reasoned that this type of screenings based on complex landscapes of genetic mutations will become more and more present in the evolving scenario of predictive medicine. Thus, the company Dedalus Italia S.p.A. designed the model and the software for implementing these screening studies in the Health Services. The project' name is "SInISA"*. The experimentation is carried out in the territory of the Regional-Health-Service (ASL5) of Eastern Liguria (Italy), with the aim of verifying and evaluating both the organizational model and the technological infrastructure to support it, with the ambition of initially sequencing the DNA with a panel of about 90 genes. The first step was to identify subjects with higher probability of bearing mutations. The first screening element will be the RDW parameter. Subjects with RDW > 15 have higher probability of bearing mutations in blood cells. It was calculated that to identify individuals with RDW > 15 it is necessary start from a population of approx. 12000 subjects This study is based on the free and voluntary participation of